

WHAT IS CLAIMED IS:

1. A novel protein having the following physicochemical characteristics and biological activity:

- (a) affinity: specifically binds to osteoclastogenesis inhibitory factor (OCIF) and exhibits high affinity to OCIF (dissociation constant on cell membrane:  $K_d = 10^{-9}$  M or less);
- (b) molecular weight: has a molecular weight of about 30,000-40,000 or about  $40,000 \pm 4,000$  when measured using SDS-polyacrylamide electrophoresis under non-reducing conditions and an apparent molecular weight of about 90,000-110,000 when cross-linked to a monomer-type OCIF; and
- (c) biological activity: exhibits activity supporting or promoting osteoclasts differentiation and maturation in a co-culture system of the osteoblastic stromal cells and spleen cells in the presence of such stimulating factors of bone resorption as active-form vitamin  $D_3$  and parathyroid hormone (PTH).

2. A process for the preparation of the protein of claim 1, comprising culturing cells of an osteoblast-like cell line or stromal cells originating from bone marrow, in the presence of stimulating factors of bone resorption, preparing a membrane fraction of the cells, solubilizing the membrane protein using a detergent, and purifying the protein using an OCIF-immobilized affinity column.

3. A screening method using the protein of claim 1 for

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a substance which specifically binds to the protein of claim 1 and inhibits or modulates the biological activity of this protein.

4. A screening method using the protein of claim 1 for a substance which specifically binds to the protein of claim 1 and transmits the biological activity of this protein.

5. A pharmaceutical composition containing the substance obtained by the screening method described in claim 3 or 4.

6. An antibody to the protein of claim 1.

7. An agent for treating bone metabolism abnormality comprising the antibody of claim 6 as an active component.

8. A DNA encoding the amino acid sequence of Sequence ID No. 1 in the Sequence Table.

9. A DNA which consists of the nucleotide sequence of Sequence ID No. 2 in the Sequence Table.

10. A DNA with one or more nucleotides deleted, substituted, added, or inserted in the nucleotide sequence of Sequence ID No. 2 in the Sequence Table, and encoding a protein capable of specifically binding to Osteoclastogenesis Inhibitory Factor and suppressing its activity.

11. A DNA which hybridizes either the DNA of claim 8 or the DNA of claim 10 under relatively mild conditions.

12. A DNA having 70% or more homology to the DNA of any one of the claims 8-11.

13. A protein obtained by the expression of the DNA of any one of the claims 8-12 by genetic engineering technique.

14. A protein of claim 13 which exhibits the activity to support and promote osteoclast differentiation or maturation.

15. The protein having the amino acid sequence of Sequence ID No. 1 in the Sequence Table.

16. A process for producing a protein by genetic engineering technique using the DNA of any one of the claims 8-12.

17. A screening method for a substance which controls expression of the protein encoded by the DNA of any one of the claims 8-12.

18. A screening method for a substance which specifically binds to the protein encoded by the DNA of any one of the claims 8-12 and inhibits or modulates its biological activity.

19. A screening method for a substance which specifically binds to the protein encoded by the DNA of any one of the claims 8-12 and transmits the biological activity of this protein through the binding.

20. A pharmaceutical composition comprising the substance obtained by the screening method described in claims 17-19.

21. A DNA encoding the protein including the amino acid sequence consisting of the amino acid residues from No. 76 to No. 316 of Sequence ID No. 1 in the Sequence Table, or according to a fragment, analogue, or variant of the protein.

22. A DNA encoding the protein including the amino acid

sequence consisting of the amino acid residues from No. 72 to No. 316 of Sequence ID No. 1 in the Sequence Table, or encoding a fragment, analogue, or variant of the protein.

23. A DNA encoding the protein including the amino acid sequence of Sequence ID No. 1 in the Sequence Table, or a fragment, analogue, or variant of the protein.

24. The DNA of any one of the claims 21-23, which encodes a protein specifically binding to Osteoclastogenesis Inhibitory Factor, OCIF, and exhibiting the activity of suppressing its biological activity.

25. A DNA of any one of the claims 21-24 which has a nucleotide sequence of Sequence ID No. 2 in the Sequence Table.

26. A DNA which hybridizes the DNA of any one of claims 21-25 under relatively mild conditions.

27. A DNA having 70% or more homology to the DNA of any one of claims 21-26.

28. A protein including a polypeptide which is obtained by expression of the DNA of any one of the claims 21-27 by genetic engineering technique.

29. The protein of claim 28 exhibiting a biological activity to support and promote the osteoclast differentiation and maturation.

30. A protein of claim 28 or 29 including the amino acid sequence of Sequence ID No. 1 in the Sequence Table, or a fragment, analogue, or variant of the protein.

31. A process for producing a protein by genetic engineering technique using the DNA of any one of the claims

21-27.

32. A screening method for a substance which controls expression of the protein encoded by the DNA of any one of the claims 21-27.

33. A screening method for a substance which specifically binds to the protein encoded by DNA of any one of the claims 21-27 and inhibits or modulates its biological activity.

34. A screening method for a substance which specifically binds to a protein encoded by the DNA of any one of claims 21-27 and transmits the biological activity of this protein through the binding.

35. A pharmaceutical composition comprising the substance obtained by the screening method of any one of claims 32-34.

36. A DNA encoding the protein including the amino acid sequence of Sequence ID No. 11 in the Sequence Table, or a fragment, analogue, or variant of the protein.

37. The DNA of claim 36, which encodes a protein specifically binding to Osteoclastogenesis Inhibitory Factor, OCIF, and exhibiting the activity of suppressing its biological activity.

38. A DNA of any one of claims 36-37 which has a nucleotide sequence of Sequence ID No. 12 in the Sequence Table.

39. A DNA which hybridizes to the DNA of any one of claims 36-38 under relatively mild conditions.

40. A DNA having 70% or more homology to the DNA of any

one of claims 36-39.

41. A protein including a polypeptide which is obtained by expression of the DNA of any one of the claims 36-40 by genetic engineering technique.

42. A protein of claim 41 which exhibits the activity to support and promote the differentiation into and the maturation of osteoclasts.

43. A protein of claim 41 or 42 including the amino acid sequence of Sequence ID No. 11 in the Sequence Table, or a fragment, analogue, or variant of the protein.

44. A process for producing a protein by a genetic engineering technique using the DNA of any one of the claims 36-40.

45. A screening method for a substance which controls expression of the protein encoded by the DNA of any one of the claims 36-40.

46. A screening method for a substance which specifically binds to the protein encoded by the DNA of any one of claims 36-40 and inhibits or modulates its biological activity.

47. A screening method for a substance which specifically binds to the protein encoded by the DNA of any one of claims 36-40 and transmits the biological activity of this protein through the binding.

48. A pharmaceutical composition comprising the substance obtained by the screening method any one of claims 45-47.

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49. An antibody which recognizes a membrane-bound protein molecule (OBM) which binds specifically to Osteoclastogenesis Inhibitory Factor (OCIF) and/or a soluble OBM (sOBM), which is deficient in the transmembrane region.

50. The antibody of claim 49 which recognizes mouse OBM and/or mouse sOBM.

51. The antibody of claim 49 which recognizes human OBM and/or human sOBM.

52. The antibody of claim 49 which is a polyclonal antibody.

53. The antibody of claim 49 which is a monoclonal antibody.

54. A monoclonal antibody of claim 53 which has cross-reactivity to human OBM, human sOBM, mouse OBM, and mouse sOBM.

55. The monoclonal antibody of claim 53 which possesses following characteristics:

- a) molecular weight: about 150,000,
- b) subclass: IgG<sub>1</sub> or IgG<sub>2</sub>, and
- c) light chain:  $\kappa$  chain

56. A process for preparing a polyclonal antibody comprising immunizing an animal with mouse or human OBM or sOBM and purifying from blood of the animal.

57. A hybridoma which produces the monoclonal antibody of any one of claims 53-55.

58. The hybridomas with deposition numbers FERM BP-6264, FERM BP-6265, or FERM BP-6266.

59. A process for preparing a monoclonal antibody comprising cultivating the hybridoma of claim 57 or 58 to produce a monoclonal antibody in the culture broth and purifying and recovering the monoclonal antibody from the culture broth.

60. A method for measuring OBM, comprising using the antibody of any one of the claims 49-55.

61. A method for measuring sOBM, comprising using the antibody of any one of claims 49-55.

62. A method for measuring OBM or sOBM, comprising using the antibody of any one of claims 49-55 as an solid phase antibody or an enzyme-labeled antibody.

63. A pharmaceutical composition containing the antibody of any one of claims 49-55 as an active component.

64. An agent for preventing or treating bone metabolism diseases comprising the antibody of any one of claims 49-57 as an active component.